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TITLE: Trial of Naltrexone and Dextromethorphan for Gulf War Veterans' Illness

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14. ABSTRACT

Approval to separate the study into a separate dextromethorphan arm and naltrexone arm from the Department of Defense Institutional Review Board was finally obtained in February 2011. We are actively screening and enrolling subjects and are very encouraged by the response.
We anticipate that by the end of the current report period, we will have preliminary data.

15. SUBJECT TERMS
Gulf War Illness, naltrexone, dextromethorphan

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INTRODUCTION

Gulf war veterans' illnesses comprise distinct clusters of symptom-defined illnesses (1,2) for which there are neither diagnostic tests nor effective treatments. Gulf war veterans had variable exposures to a number of chemicals (3), including organophosphate insecticides, pyrethrum-related insecticides, DEET, Pyridostimine bromide, smoke from oil well fires, and Sarin gas. Gulf war veterans' illnesses may reflect an inflammatory cycle involving the brain which may be a common mechanism of many neurological conditions, whether initiated by toxic exposures, infection, or trauma. In this theory, central nervous system inflammation initiated by toxic exposures and sometimes exacerbated by subsequent exposures is a component of illness hypothesized to explain the neurological manifestations. Substance P release at sensory nerve endings is an explanation for the peripheral pain manifestations of illness.

This theory suggests that novel anti-inflammatory drugs may be of benefit in symptom-defined illnesses related to a cycle of inflammation. Dr. J. S. Hong's laboratory at the National Institute of Environmental Health Sciences has demonstrated that Morphine-related analogs, including Naltrexone and Dextromethorphan, have great potency in anti-inflammation and neuroprotective effects. Naltrexone is a safe and readily available generic medication. Dextromethorphan is also a safe and readily available generic medication that is available without a prescription as a cough medication. Results from several clinical trials showed that Naltrexone is effective in several inflammation-related diseases, such as neurogenic pain, movement disorders, etc. In addition, there were no obvious side effects in patients taking this drug for six months. This project is a randomized double-blinded studies for treating ill Gulf war veterans with Naltrexone and Dextromethorphan. Laboratory tests for markers of inflammation including neurogenic inflammation will be performed pre- and post-treatment, to see if these markers are elevated and if so, to see if treatment modulates these markers.

BODY

The major accomplishment of the past year was obtaining approval from the Department of Defense Institutional Review Board (DOD IRB) to modify the protocol to split the study into two sub-studies. The reason for this is that the original protocol required that veterans qualify to be enrolled in both the dextromethorphan arm and the naltrexone arm sequentially. A large number of screened veterans were only eligible to be enrolled in one or the other of the two arms due to their taking medications to treat Gulf War Illness which have drug interactions with one or the other study drug. This modification did not impact patient safety and could have been obtained by a one line addition to the protocol: “Subjects who only qualify to be enrolled in one arm of the study will only be enrolled in that arm.”

While this may not seem a significant accomplishment, obtaining this approval proved to be a virtually impossible task. It took one year. After finally obtaining DOD approval, we then had to obtain approval for the changes from the East Carolina University Institutional Review Board (ECU IRB) and the United Stated Food and Drug Administration (US FDA) because the study drug dextromethorphan required and IND number.

After final approval was obtained, recruitment efforts became intensive.

KEY RESEARCH ACCOMPLISHMENTS

The most significant accomplishment during the past year was finally obtaining DOD IRB approval to enroll subjects in only one arm of the protocol if they only qualify for one arm. We are now vigorously at last pursuing the study. We have enrolled thirteen subjects in the naltrexone or dextromethorphan. We have one subject who has completed the dextromethorphan arm of the study and will soon complete the naltrexone arm. We have screened a number of other subjects who qualify and have expressed a desire to participate. They have been sent the consent form to review and discuss with relatives and treating physicians before giving consent.

REPORTABLE OUTCOMES

No data has been analyzed.

CONCLUSIONS

It is very difficult to get regulatory approval to conduct research, a two or more years must be allowed for this task. At last, we are actively enrolling subjects in the protocol and are encouraged at the response.

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